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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/930,312	08/15/2001	Peter Lind	PHRM-0366	3604

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/930,312	LIND, PETER	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 23-80* is/are pending in the application.

4a) Of the above claim(s) *23, 24, 30-66 and 73-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21,25-29,67-72 and 80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21 and 23-80* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/21/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 19 November 2003 is acknowledged and entered. Following the amendment, claim 22 is canceled, claims 1, 3, 10, 12, 25-27 and 67 are amended, and the new claim 80 is added.

Currently, claims 1-21 and 23-80 are under pending, and claims 1-21, 25-29, 67-72 and 80 are under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claim 22 are moot as the applicant has canceled the claim.

The objection of the specification is withdrawn in view of applicant's argument.

The objection of claim 67 for being dependent form a non-elected claim is withdrawn in view of applicant's amendment.

The rejection of claims 1-22, 25-29 and 72 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in view of applicant's amendment.

Formal Matters:

Priority

The claims of the instant application are not entitled to the benefit of the filing date of US provisional applications 60/225,262 as it does not satisfy the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph (see the reasons of record set forth in the last Office Action, paper No. 14, mailed on 17 July 2003, at page 3).

Applicants argument filed on 19 November 2003 has been fully considered, but is not deemed persuasive for reasons below.

Objections and Rejections under 35 U.S.C. §101 and §112:

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-21, 25-29, 67-72 remain rejected, and the new claim 80 is rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, and specific, or a well-established utility, for the reasons of record set forth in the last Office Action, paper No. 14, mailed on 17 July 2003, at pages 4-5.

Applicants argument filed on 19 November 2003 has been fully considered, but is not deemed persuasive for reasons below.

At page 20 of the response, the applicant argues that the claimed invention has a **specific** utility and meets the utility requirement as uses for GPCRs include therapeutic and diagnostic uses as well as research-based uses, and GPCRs are recognized as important therapeutic targets for a wide range of diseases, and that the allegation that there is no well established utility for proteins of the class that the applicant is claiming is directly refuted by industry evidence. This argument is not persuasive because the issue is not whether GPCRs as a whole have any utility, rather, the issue is that the presently claimed nGPCR-1079 does not have a substantial, and specific, or a well-established utility. As addressed in the last Office Action, members of GPCR superfamily have extremely diverse, and sometimes even opposite biological activities and functions, even though they have an overall similar molecular structure. They manifest high functional diversity, and mediate the actions of extracellular signals as diverse as light, odorants, taste, peptide hormones, chemokines, and neurotransmitters. Therefore, there is no way that one can predict any functional property of a GPCR merely based on its GPCR structure.

At page 21 of the response, the applicant argues that it is not true that inventions useful for use in research are unpatentable as many US patents claim useful research tools, that *Brenner* excludes only those research purposes where the only use of the material itself is as the subject of research, and that assay methods such as identifying chemical compounds clearly have "real world" value. This argument is not persuasive because the patented research tools are not used to further research themselves, whereas the instant GPCR does not have an immediately apparent or fully disclosed "real world" utility. The asserted utility in diagnosis and treatment is not specific as there is no knowledge of the ligands which said nGPCR-1079 binds, or any disclosed

gene mutation, or any disease or condition which could be so diagnosed, or treated. With respect to assay methods, use of a protein in screening assays in general is not considered a specific or substantial utility in the absence of a specific use for such a protein, as such use could be asserted for *any* protein, according to MPEP, which states that ***a "specific utility"*** is specific to the subject matter claimed, this contrasts with a *general* utility that would be applicable to the broad class of the invention, and that labels such as "research tool," ... are *not helpful* in determining if an applicant had identified a specific and substantial utility for the invention" (MPEP 2107.01, pages 2100-32 and 33).

At pages 22-23 of the response, the applicant argues that because all GPCRs, as a class, convey practical benefit (much like the class of DNA ligases identified in the Training Materials), there should be no need to provide additional information about them, that applicants need only prove a "substantial likelihood" of utility, certainty is not required, and that a patent applicant's assertion of utility in the disclosure is presumed to be true and correct. Applicants further argue that the present GPCR is related to GPCRs, and the Office has not provided evidence or sound scientific reasoning that one skilled in the art would doubt the "reasonable correlation" advanced by applicant, and that the present application recites that the claimed invention can be used to identify ligands, protein binding partners and modulators, and the polynucleotide (polypeptide?) can be used to generate antibodies. These arguments are not persuasive for the following reasons. First, as addressed above, the issue is not whether GPCRs as a class have utility, rather, the issue is that the presently claimed *nGPCR-1079* does not have a substantial, and specific utility. The situation in GPCRs is completely different from that of DNA ligases because the main function of DNA ligases is to ligate DNA regardless of different molecules of DNA ligases, whereas GPCRs are extremely diverse with respect to their functional properties. Further, it is not that the Office is in doubt of applicants assertion of specific and substantial utility, rather, it is that there is no such utility ever disclosed in the present application. Uses in identifying ligands, protein binding partners and modulators, and generating antibodies are not considered by the Patent Office to be a specific or substantial utility in the absence of a specific use for such ligands, modulators, or antibodies, as such use could be asserted for *any* protein.

At page 24 of the response, the applicant argues that in contrast to the invention in *Brenner*, GPCRs related to known GPCRs stand on a very different basis as there are a multitude of utilities for the claim polypeptides, including their ability to facilitate research, and that polypeptides of all types are broadly used in the biotechnology industry, playing key roles in drug and disease processes. This argument is not persuasive for the same reasons above, i.e., it is the claimed nGPCR-1079, not GPCRs in general, must have a specific and substantial utility.

At page 25 of the response, the applicant argues that the claimed invention has a **substantial** utility as applicant teaches that the claimed invention can be used to make antibodies, identify ligands and binding partners, and thus has real world uses. This argument is not persuasive because, as addressed above, these uses are not considered by the Patent Office to be a specific or substantial utility in the absence of a specific use for the identified compounds or antibodies. A ***substantial utility***, by definition, is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility. In the instant case, without knowing the specific functional property, or biological significance of said nucleic acid or the polypeptide encoded thereby, nor their association to a specific disease or condition, one of skilled in the art would not know how to use the antibodies, or the compounds resulted from the screening assay, what it can be so diagnosed or treated using the nucleic acid, the polypeptide or the compound. Therefore, there was no "real world" use for the claimed nucleic acid as of the filing date. Upon further research, a specific, and substantial utility might be found for the claimed isolated nucleic acid or the protein encoded thereby. This further characterization, however, is part of the act of invention, and until it has been undertaken, the claimed invention is incomplete.

At pages 26-29 of the response, the applicant argues that the utility requirement may also be satisfied by an "Art Established Utility", and cites a number of US patents which subject matter is GPCRs. Applicants further argue that Applicant does not determine function based on the structure of the protein, rather the prediction is based upon the sequence similarity with known polynucleotides or polypeptides, that it is well known that the probability that two unrelated polypeptides share more than 40% sequence homology is exceedingly small, and the probability that the polypeptide encoded by the claimed polynucleotides is related to the reference polypeptides is accordingly very high. This argument is not persuasive for the

following reasons. With respect to the cited US patents, once again, the issue remains the same, that is that it is the instant nGPCR-1079 or the encoding nucleic acid, not GPCRs in general, must have a specific and substantial utility, and the present specification fails to disclose such. With respect to the sequence similarity, generally the art acknowledges that function cannot be predicted based solely on structural similarity to a known protein. For example, Doerks et al. (1998, Trends in Genetics 14:248-250) states that overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remarks that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Further, Yan et al. (Science, 2000, 290:523-527) discloses two isoforms of EDA polypeptides, EDA-A1 and EDA-A2, differing by an insertion of two amino acids, which results in their difference in receptor binding specificity (the abstract). Therefore, higher % sequence homology between two polypeptides may indicate that they are related, or belong to the same family, however, it does not mean that they have the same functional properties. In the instant case, the nGPCR-1079 may well be a GPCR, which, however by itself, does not automatically confer any specific and substantial utility because the members of the GPCR family have extremely diverse functional properties.

Note: the newly cited references are merely used to rebut applicants arguments, and it is not for sustaining any new ground of rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-21, 25-29 and 67-72 remain rejected, and the new claim 80 is rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, substantial or credible utility for the reasons set forth above, one skilled in the art

clearly would not know how to use the claimed invention, for the reasons of record set forth in the last Office Action, paper No. 14, at page 5.

Applicants argument filed on 19 November 2003 has been fully considered, but is not deemed persuasive for reasons addressed above.

Furthermore, even if the specification taught how to use the nGPCR-1079, enablement would not be commensurate in scope with the claims, which encompass nucleic acids of SEQ ID NO:1, nucleic acids encoding SEQ ID NO:2, and variants thereof (% variants, allelic variants, and hybridization variants, claims 1, 3, 67, 69 and 80, for example). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with the claims. The specification discloses merely one nucleic acid with SEQ ID NO:1 encoding a polypeptide of SEQ ID NO:2, or nGPCR-1079, and provides neither guidance, nor working example to teach how to make any of variants of nGPCR-1079. Further, the specification does not define any functional domain or region in nGPCR-1079, nor, in fact, has any specific biological activity been disclosed for nGPCR-1079. Without knowing what the biological activity is, one skilled in the art would not be able to test any variant for the its function, and it would require undue experimentation to make a variant conserving the biological activity. Additionally, the skilled artisan would not know how to use the variants encoding inactive polypeptides as there is no functional limitation associated with the variants.

Claims 1-22, 25-29 and 67-72 remain further rejected, and the new claim 80 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the last Office Action, paper No. 14, at pages 8-9.

Applicants argument filed on 19 November 2003 has been fully considered, but is not deemed persuasive for reasons below.

At page 31 of the response, the applicant argues that although the disclosed sequence may not be full length GPCRs, there is no indication that the present sequence possess no

function, or that the sequences cannot be used for other purposes such as raising antibodies and identifying binding partners even if they do not retain GPCR activity, and that experiments or assays such as enzymatic assays to measure GPCR function are routine and well known in the art. This argument is not persuasive because the art has not established that a 1/3 fragment of a GPCR is likely to possess any functional activity, and the present application fails to demonstrate any activity associated with the nGPCR-1079. Additionally, binding activity of a GPCR requires the presence of certain regions of the molecule, and the present specification does not provide any indication that the 1/3 fragment of the GPCR comprises such regions and is capable of binding to a ligand. Additionally, the issue is not whether the assays are routine, rather, it is that one of skill in the art would not know how to make the full length or functional polypeptide and how to use the one without functional activity. With respect to the use in raising antibodies and identifying binding partners (if the fragment possessed the binding activirty), as the functional activity or biological significance of the polypeptide is unknown, the issue is, once again, how to use the antibodies and the binding partners identified besides further research of the polypeptide itself.

Claims 1-4, 8, 22, 27, 67, 69, 71 and 72 remain rejected, and the new claim 80 is rejected rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the last Office Action, paper No. 14, at pages 6-7.

Applicants argument filed on 19 November 2003 has been fully considered, but is not deemed persuasive for reasons below.

At page 32 of the response, the applicant argues that the claims have been amended to recite a specific level of homology, and a skilled artisan can readily envision the structure of the claimed polypeptides and nucleic acids based on the present application. This argument is not persuasive for the following reasons. The present specification discloses a nucleic acid encoding a polypeptide sequence of a previously unknown protein, and fails to disclose any specific biological function associated with the protein. Written description of the detailed chemical structure of the encompassed variants and fragments of the nGPCR-1079 of SEQ ID NO:2 is

particularly important in absence of a specific known activity because one of skill in the art would have no basis to derive the claimed ranges (variants and fragments in the instant invention) from the disclosure, and thus, would not be able to envision the detailed chemical structure of the encompassed, or to make any meaningful predictions of the useful variants and fragments of the protein.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In the instant case, the only factor present in the claims is a partial structure of a GPCR in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Rejections Over Prior Art:

The following rejections under 35 U.S.C. § 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 8/15/01, which is the actual filing date of the instant application.

Applicants argument filed on 19 November 2003, regarding the priority date has been fully considered, but is not deemed persuasive for reasons addressed under "Priority" above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1-21, 25-29 and 67-71 remain rejected, and the new claim 80 is rejected under 35 U.S.C. 102(e) as being anticipated by Paszty et al., US 2002/0123618, for the reasons of record set forth in the last Office Action, paper No. 14, at pages 10-11.

Applicants argument that the effective filing date of the present application is August 15, 2000 (the filing date of the provisional application 60/225,262), and that the reference fails to predate such is not persuasive for the reasons cited above.

Claims 1-9, 13, 16, 20-22, 25, 26, and 69-71 remain rejected, and the new claim 80 is rejected under 35 U.S.C. 102(a) as being anticipated by Chen et al., WO 01/36471, for the reasons of record set forth in the last Office Action, paper No. 14, at pages 11-12.

Applicants argument that the effective filing date of the present application is August 15, 2000 (the filing date of the provisional application 60/225,262), and that the reference fails to predate such is not persuasive for the reasons cited above.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10-12, 14, 15, 17-19, 27-29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al., WO 01/36471 (25 May 2001), as applied to claims 1-9, 13, 16, 20-22, 25, 26, 69-71 and 80 above, and further in view of Glucksmann et al., US 5,945,307, for the reasons of record set forth in the last Office Action, paper No. 14, at pages 12-13.

Applicants argument that the effective filing date of the present application is August 15, 2000 (the filing date of the provisional application 60/225,262), and that the reference fails to predate such is not persuasive for the reasons cited above.

Conclusion:

No claim is allowed.

Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
2/17/04